

FILE 'MEDLINE, CAPLUS, BIOSIS, AGRICOLA' ENTERED AT 14:25:55 ON 15 APR  
2004

L1        110704 S HETEROCYCLIC  
L2        339 S P450BM-3 OR P450BM3 OR P450BM  
L3        3 S L2 AND L1  
L4        2 DUP REM L3 (1 DUPLICATE REMOVED)  
L5        0 S P450 NEAR3 BM  
L6        370 S P450 AND MEGATERIUM  
L7        5 S L6 AND L1  
L8        3 DUP REM L7 (2 DUPLICATES REMOVED)  
L9        574 S P450 AND L1  
L10      80 S L9 AND OXIDATION  
L11      35 S L10 AND AROMATIC  
L12      23 DUP REM L11 (12 DUPLICATES REMOVED)  
L13      689 S PAH AND P450  
L14      901 S PAH AND P450?  
L15      1 S L14 AND P450BM-3  
L16      1 S L14 AND P450BM?

L12 ANSWER 7 OF 23 MEDLINE on STN DUPLICATE 4  
AN 1998372714 MEDLINE  
DN PubMed ID: 9705755  
TI Activation of **heterocyclic aromatic** amines by rat and human liver microsomes and by purified rat and human cytochrome **P450** 1A2.  
AU Turesky R J; Constable A; Richoz J; Varga N; Markovic J; Martin M V; Guengerich F P  
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NC P30 ES00267 (NIEHS)  
R35 CA44353 (NCI)  
SO Chemical research in toxicology, (1998 Aug) 11 (8) 925-36.  
Journal code: 8807448. ISSN: 0893-228X.  
CY United States  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals  
EM 199809  
ED Entered STN: 19981008  
Last Updated on STN: 19981008  
Entered Medline: 19980928  
AB The dietary mutagens 2-amino-3,8-dimethylimidazo[4,5-f]quinoxaline (MeIQx) and 2-amino-1-methyl-6-phenylimidazo[4,5-b]pyridine (PhIP) are activated to genotoxins by rat and human liver cytochrome **P450** (P450) 1A1- and 1A2-mediated **N-oxidation**. Immunoquantitation of 51 human liver samples revealed a wide range in **P450** 1A2 expression (10-250 pmol/mg of microsomal protein, median 71 pmol/mg), with 39% of the livers containing >100 pmol/mg of protein. There was no evidence for expression of **P450** 1A1 (<1 pmol/mg of protein). **P450** 1A2 levels were correlated to MeIQx and PhIP **N-oxidation** rates ( $r = 0.83, 0.73$ , respectively). In male Fischer-344 and Sprague-Dawley rats, hepatic **P450** 1A2 ranged from 5 to 35 pmol/mg of protein, while **P450** 1A1 was <1 pmol/mg. Animal pretreatment with 3-methylcholanthrene, beta-naphthoflavone, or polychlorinated biphenyls (PCB) resulted inasmuch as 340-fold and >1000-fold induction of **P450** 1A2 and 1A1, respectively, and a 220-fold increase in **N-oxidation** activity. Approximately 20% of the human samples were as active in **N-oxidation** and conversion of MeIQx to bacterial mutagens as microsomes of PCB-pretreated rats [3-4 nmol of HNOH-MeIQx formed min-1 (mg of protein)-1]. In contrast, microsomes from PCB-treated rats displayed higher rates of PhIP **N-oxidation** and activation to mutagens than the most active human liver microsomes [8-24 vs 2-4 nmol of HNOH-PhIP formed min-1 (mg of protein)-1]. Recombinant human **P450** 1A2 showed catalytic efficiencies of MeIQx and PhIP **N-oxidation** that were 10-19-fold higher than purified rat **P450** 1A2. Cytochrome **P450** 1A2 expression in rodent and human liver tissue varies greatly and there are considerable differences between the enzymes in the two species in the activation of some **heterocyclic aromatic** amines, which must be considered when assessing human health risk.